Supplementary Materials

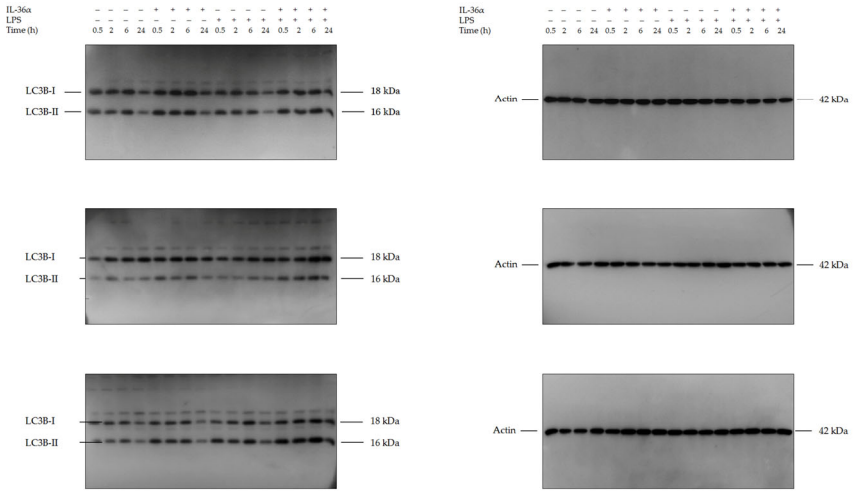

Figure S1. IL-36*α* and LPS cooperatively increase the level of LC3B-II.

Western blot images used to calculate the fold changes of LC3B-II shown in Figure 2B.

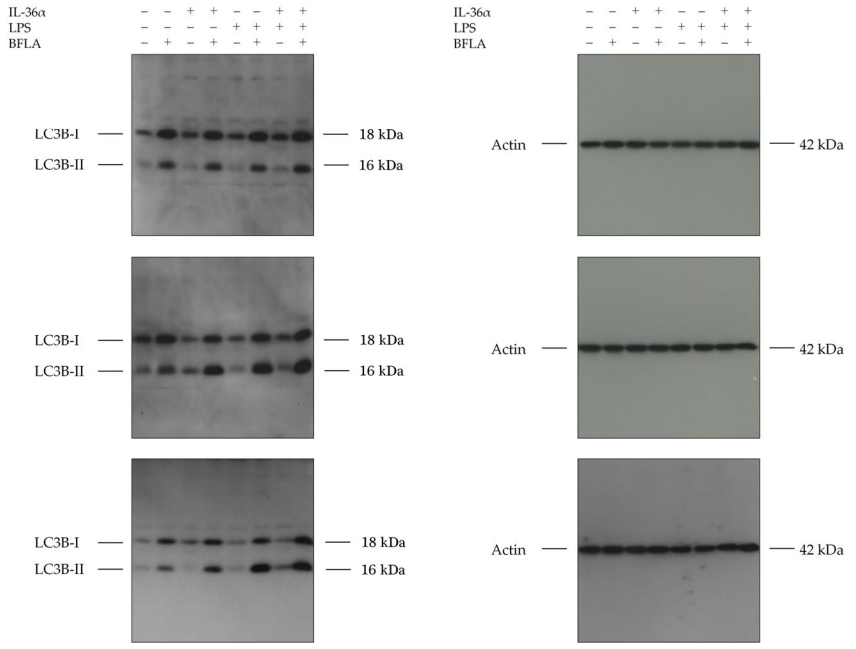

Figure S2. IL-36*α* and LPS cooperatively stimulate the autophagic flux.

Western blot images used to calculate the fold changes of LC3B-II shown in Figure 3B.

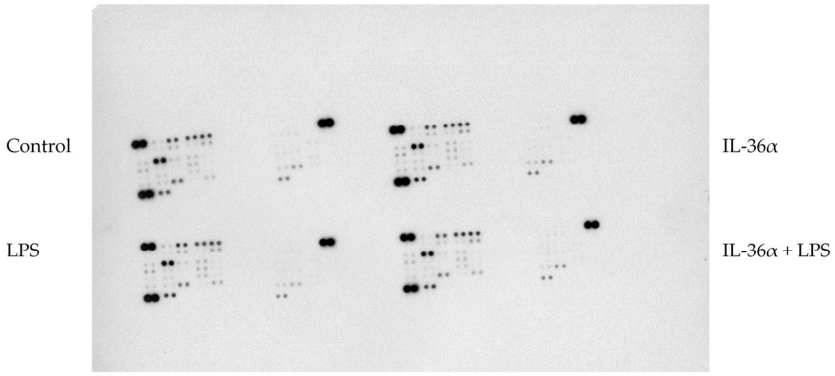

Figure S3. Differential phospho-kinase array profiles of cells treated with IL-36α and LPS.

Uncropped image of the phospho-kinase array used to create Figure 5.

Table S1. List of the detected phospho-proteins by using the Proteome Profiler™ human phospho-kinase array kit.

Membrane/ Coordinate	Target/Control	Phosphorylation Site
A-A1, A2	Reference Spot	-
A-A3, A4	p38α	T180/Y182
A-A5, A6	ERK1/2	T202/Y204, T185/ Y187
A-A7, A8	JNK1/2/3	T183/Y185, T221/ Y223
A-A9, A10	GSK-3α/β	S21/S9
B-A13, A14	p53	S392
B-A17, A18	Reference Spot	-
A-B3, B4	EGFR	Y1086
A-B5, B6	MSK1/2	S376/S360
A-B7, B8	AMPKα1	T183
A-B9, B10	Akt 1/2/3	S473
B-B11, B12	Akt 1/2/3	T308
B-B13, B14	p53	S46
A-C1, C2	TOR	S2448
A-C3, C4	CREB	S133
A-C5, C6	HSP27	S78/S82
A-C7, C8	AMPKα2	T172
A-C9, C10	β-Catenin	-
B-C11, C12	p70 S6 Kinase	T389
B-C13, C14	p53	S15
B-C15, C16	c-Jun	S63
A-D1, D2	Src	Y419
A-D3, D4	Lyn	Y397
A-D5, D6	Lck	Y394
A-D7, D8	STAT2	Y689
A-D9, D10	STAT5a	Y694
B-D11, D12	p70 S6 Kinase	T421/S424
B-D13, D14	RSK1/2/3	S380/S386/S377
B-D15, D16	eNOS	S1177
A-E1, E2	Fyn	Y420
A-E3, E4	Yes	Y426
A-E5, E6	Fgr	Y412
A-E7, E8	STAT6	Y641
A-E9, E10	STAT5b	Y699
B-E11, E12	STAT3	Y705
B-E13, E14	p27	T198
B-E15, E16	PLC-γ1	Y783
A-F1, F2	Hck	Y411
A-F3, F4	Chk-2	T68
A-F5, F6	FAK	Y397
A-F7, F8	PDGF Rβ	Y751
A-F9, F10	STAT5a/b	Y694/Y699
B-F11, F12	STAT3	S727
B-F13, F14	WNK1	T60
B-F15, F16	PYK2	Y402
A-G1, G2	Reference Spot	-

A-G3, G4	PRAS40	T246
A-G9, G10	PBS (Negative Control)	-
B-G11, G12	HSP60	-
B-G17, G18	PBS (Negative Control)	-

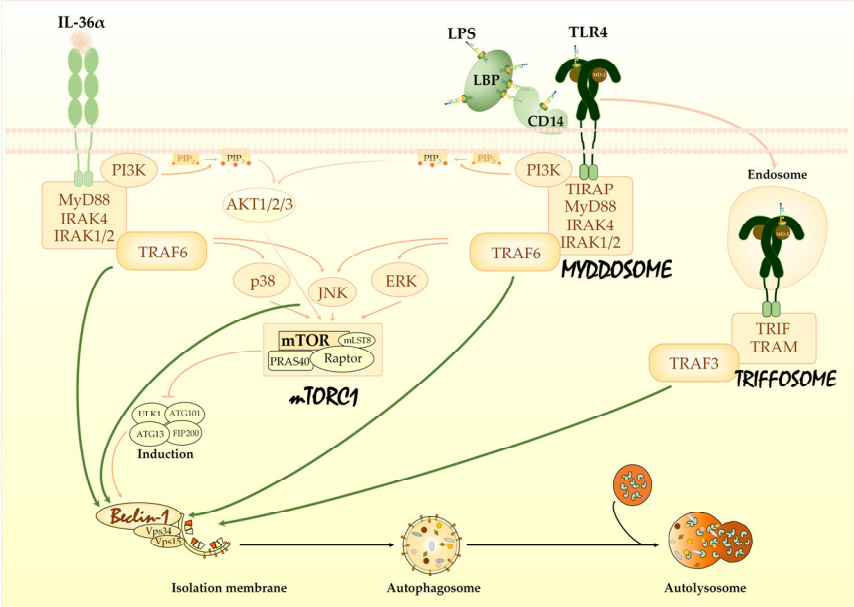

Figure S4. IL36α and LPS cooperatively induced autophagy by multiple mechanisms.

The IL-36α/LPS combination reduces the activation level of the PI3K/Akt/mTORC1 axis by triggering rapid depletion of PIP2 at the cytoplasmic membrane. As a result, mTOR-mediated inhibition of autophagy is alleviated. Additionally, the IL-36α/LPS combination increases the activation level of PI3KC3 complex via the activation of MyD88, TRAF3, and TRAF6. As a result, autophagosome formation is stimulated. Thus, this cytokine/PAMP combination triggers pro-autophagic biased signaling by several mechanisms and thereby stimulates the autophagic cascade cooperatively.